

I. Rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement. Claims 35, 36, 39-43, and 46-51 stand rejected under 35 USC § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant submits that the disclosure of the Application is sufficient to allow a chemist of ordinary skill to make and use the claimed boroproline-containing L isomers, and paragraphs 7-8 of the Declaration of Robert R. Rando support the Applicant's position. Rando concludes at the end of paragraph 8 "that there remained uncertainties regarding the utility of conventional silica gel chromatography described on page 15 for separating the L and D isomers but that the HPLC method described on page 21 of the application would be useful for this purpose." Since the specification teaches one of ordinary skill in the art how to make and use the claimed invention as evidenced by the Rando Declaration, Applicant respectfully requests that the rejection be removed.

II. Rejection under 35 U.S.C. § 112, first paragraph, for lack of written description. Claims 35, 36, 39-43, and 46-51 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Examiner contends that there is no support in the specification for stereochemical purities of 96% and 99% with respect to the carbon atom bearing boron. Applicant submits that there is adequate written description support for 96% and 99% stereochemical purity. In support of the Applicant's position, Rando states in paragraph 9 of the Declaration submitted herewith that "the expression '99-6%' is consistent with an interpretation that the phrase '99-6%' refers to a range of about 96% to 99%." Reconsideration and withdrawal of the rejection of the pending claims under 35 U.S.C. § 112 is respectfully requested.

III. Rejection under 35 U.S.C. §103, as being unpatentable over the prior art. Claims 35, 36, 39, 41, 42, 46, and 47 have been rejected under 35 U.S.C. § 103, as being unpatentable over

invention is obvious over the Bachovchin JBC reference, and in support of Applicant's position, a Declaration under 37 C.F.R. § 1.132 of Robert R. Rando, the Gustavus Adolphus Pfeiffer Professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School, Boston, Massachusetts, is submitted herewith. In paragraph 6 of the Declaration, Rando concludes "that the Bachovschin JBC reference does not disclose the purification of an L-isomer of a boroproline-containing peptide using silica gel or any other method."

The Declaration evidences in paragraph 10, that since the boroproline-containing peptides of the claimed invention are designed for therapeutic use, that one of ordinary skill in the art would not have been even motivated to isolate the L-isomer, but rather would have focused his or her efforts on the D-isomers given the longer half-life *in vivo* of the D-isomers. Rando in paragraph 11 of the Declaration also states that it would not have been possible to know in advance which method out of the many available to separate stereoisomers would be useful for the purpose of separating the diastereomers of the claimed invention. Rando also adds that one would not have had a reasonable expectation that the HPLC C18 chromatography method would be successful in achieving the purification of the L-isomer. In light of this additional evidence, Applicant requests that the rejection under § 103 be withdrawn.

In view of the forgoing arguments, Applicant respectfully submits that the present case is now in condition for allowance. A Notice to that effect is requested.

Please charge any fees that may be required for the processing of this Response, or credit any overpayments, to our Deposit Account No. 03-1721.

Respectfully submitted,



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